Lovaxin C

Paving the Way for Listeria-based Cancer Vaccines

Yvonne Paterson
Professor, Department of Microbiology
at the University of Pennsylvania School of Medicine;
Chair, Scientific Advisory Board Advaxis Inc

The most common methods for fighting cancer are brutal and aggressive. Surgery, chemotherapy and radiation result in cutting, bruising, burning and scarring. In sharp contrast, vaccines are designed to nudge the body to heal itself. For years, scientists in labs around the world have worked toward discovering and developing vaccines that would activate the body’s ability to destroy malignant tumors. Lovaxin C, a live vaccine from Advaxis Inc, does that — with fewer costs and difficulties than autologous vaccines.

Live vaccines have been created, subsequent to the development of autologous vaccines, and are more cost-effective. Autologous vaccines are formulated around two concepts. The first is that each patient’s immune system and immune response to cancer is unique. Thus, to stimulate the immune system to effectively cure cancer it is necessary to collect and use a patient’s own tumor cells. These cells are then bio-engineered to target immune recognition. This line of research has advanced our understanding of cancer and the immune system, and facilitated some success in the development of novel therapeutic agents and methodologies, but it has not lead to widespread cancer cures. Custom-made, patient-specific agents are expensive (some therapies are quoting costs of more than $50,000 per dose), and their development procedures raise yet unresolved regulatory considerations.

Conversely, live-vaccine therapy is founded on the notion that the manner in which antigens are presented to the immune system may be as important as the antigens themselves. Thus, a common antigen expressed in cancer, not unique to a specific patient, could be used to mount a therapeutically effective immune response if properly presented to the immune system. A recent variation of this approach recognizes that the immune system has evolved to deal with infections, as opposed to peptides, pieces of DNA, antibodies, or even cells that are removed from patients, activated, and returned. This has led to the exploration of bioengineering relatively harmless microbes to express cancer antigens. In this way, it might be possible to administer a modified microbe to a cancer patient to invoke an infection
that generates a strong immune response, not only curing the cancer but also generating a long-lived immunity that prevents cancer recurrence once the infection passes. These agents are called live vaccines.

At Advaxis we are engaged in such research using the microbe Listeria monocytogenes (Lm), which has uniquely evolved in a way suitable for this purpose. Listeria is a common pathogen with which humanity has an immune relationship, since we routinely ingest it, typically in dairy products. It does occasionally cause disease (usually food poisoning) when ingested in the large amounts found in spoiled food, or by immuno-compromised people. Since Listeria is a bacterium, it strongly stimulates “innate” (non-specific) immunity: a strong activator of adaptive immune responses directed against specific targets. Lm preferentially infects Antigen Processing Cells (APC). These are cells in which antigens are processed to create the recognition molecules that stimulate the immune system to identify and kill specific invaders. Lm, therefore, can directly target cancer antigens to these cells and to the cellular compartment in which the recognition molecules are made. We have engineered specific types of fusion proteins that target the delivery of the cancer antigens Lm secretes. The delivery of the antigen as a fusion protein dramatically increases the cellular response to these antigens, more so than would be induced by the antigen alone. This results in the activation of an unusually high level of cytotoxic lymphocytes to kill the specific tumor that displays the engineered antigen. Clearly, the Lm delivery system does not require the difficult and expensive processes associated with autologous vaccines.

Our first agent to reach the clinic, targets an antigen displayed in approximately 50% of cervical cancers. If the treatment is effective, the same agent could be used in all women afflicted with a cancer expressing the target antigen. In many experiments with animals, our response rate has been 100%, with complete responses varying from 50% to 100%. The confirmation of these findings in human subjects would validate this method of antigen delivery — that non-patient-specific therapy yields significant therapeutic responses perhaps exceeding those produced using autologous methods.

At present, Advaxis’ foremost cause is cervical cancer, the world’s leading cancer killer of women between the ages of 25 and 50. We are confident that Lovaxin C will prove effective during all stages of the cervical cancer pathway, from the early to the intermediate to the late stage. Once this development program is established, the Company intends to initiate clinical research programs using Lovaxin as a treatment for additional forms of cancer.

Contact Details:
Contact Person: Yvonne Paterson, Ph.D.
Professor of Microbiology
Associate Dean for Postdoctoral Research Training
Director of Biomedical Postdoctoral Programs
Address: University of Pennsylvania
323 Johnson Pavilion
36th St. and Hamilton Walk
Philadelphia, PA 19104-6076
Tel: +1 215 898 3461
Fax: +1 215 573 4666